OBJECTIVES:

To provide an understanding of the history, progress, and future of the National Cancer Program.

DATA SOURCES:

Published articles, reports, book chapters, and the National Cancer Institute (NCI) web site.

CONCLUSIONS:

The NCI is the largest agency for cancer research. The cancer incidence and burden remains significant in spite of many advances. Oncology nurses can contribute to the prevention and cure of cancer through an enhanced understanding of the NCI's program.

IMPLICATIONS FOR NURSING PRACTICE:

The NCI provides many opportunities for oncology nurses. Nurses can conduct NCI-sponsored research trials, serve on NCI advisory boards, and participate in clinical research. Nurses can advise patients and the public of the many resources available to patients from the NCI and assist patients with informed decision making.

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THE NATIONAL CANCER PROGRAM

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THE National Cancer Institute (NCI), the federal government's largest agency for cancer research, leads the nation's fight against this challenging disease. The NCI supports and conducts innovative research on many aspects related to cancer, such as biology, etiology, detection, treatment, and survivorship. The impact of the National Cancer Program is illustrated by an extraordinary record of scientific discovery in cancer research. Better prevention, detection, and treatment strategies, however, are desperately needed. The revolution in molecular biology and genetics and the emergence of powerful new technologies are providing opportunities to generate new knowledge and develop new strategies for cancer control. Although many advances have been made, the cancer burden in the United States remains a significant public health problem. Through an enhanced understanding of the NCI's mission, priorities, and programs, oncology nurses will be better prepared to contribute further to the ultimate goal: preventing and curing all forms of cancer.

EVOLUTION OF THE NATIONAL CANCER PROGRAM

National Cancer Institute Act

On August 5, 1937, President Franklin D. Roosevelt signed into law the National Cancer Institute Act, establishing the NCI as an agency within the Public Health Service.[1,2] The Act directed the Surgeon General to promote coordination of research conducted by the NCI and other agencies, organizations, and individuals. In 1944, the Public Health Service Act consolidated much of the nation's health efforts, including designating the NCI as part of the National Institutes of Health (NIH).

During the 30 years after the creation of the NCI, several important advances were made. The era of cancer chemotherapy began in the 1940s with the introduction of nitrogen mustard. Nitrogen mustard was developed as a derivative of mustard gas, the poison gas that was used in World War I. Nitrogen mustard was developed as an antineoplastic agent after it was learned that soldiers exposed to mustard gas drug developed reversible leukopenia. It proved to have remarkable activity against the lymphomas and served as a model for the development of other

alkylating agents, such as cyclophosphamide and melphalan. Following the introduction of nitrogen mustard, aminopterin (the predecessor of methotrexate) and other antimetabolites such as 6-mercaptopurine and 5-fluorouracil were developed and used for the treatment of advanced cancer. In the 1960s, another class of cytotoxic therapy, the platinum-coordinated complexes, was introduced. Significant advances occurred in cancer etiology as well. While the smoking and cancer link was first noted in the 1930s, the first analytical epidemiologic study linking smoking with lung cancer was not published until 1950.[3] This led to the landmark Surgeon General's report on smoking and health in 1964.[4]

National Cancer Act

Historic legislation in the federal effort to fight cancer was passed on December 23, 1971, when President Richard M. Nixon signed the National Cancer Act[1,2] (Table 1). This Act was signed into law to greatly expand and intensify a "coordinated cancer research program encompassing the programs of the NCI, related programs of other research institutes, and other federal and nonfederal programs."[5] The passage and signing of the National Cancer Act stimulated the greatest concerted effort for the control of cancer in history, a commitment that had never been made by any other country.[6] The Act, which mandated resources and authority for NCI to make "conquest of cancer a national crusade," is one of the most successful and sustaining pieces of federal legislation ever passed.[7] Proponents of the Act advocated increased emphasis on the application of research results to improve methods of cancer detection, treatment, prevention, and control for the general public.[8] It was anticipated that this federal "war on cancer" would find quick success. The NCI Director, Dr Carl G. Baker, was charged with the overall coordination and responsibility of what has come to be called the National Cancer Program. The President's Cancer Panel was created to monitor its implementation and to report any delays or barriers to its progress directly to the President.

In 1971, very little was known about complex mechanisms involved in cancer, such as the progression of a normal cell into a tumor cell or how tumor cells multiply and metastasize. It was believed that cancer could be conquered through information dissemination and cancer control programs designed to bring the benefits of knowledge to all Americans. At that time, knowledge about cancer and treatment options was limited.

TABLE 1.

1971 National Cancer Act

The 1971 National Cancer Act authorized the NCI to carry out a national cancer program which ensured that

- The program be developed by the NCI Director with the advice of the National Cancer Advisory Board, a presidentially appointed committee of 18 members, including both distinguished scientists and lay persons from the community at large. The National Cancer Advisory Board has 12 ex officio members from other government agencies.
- A three-member panel, the President's Cancer Panel, appraised the program by holding periodic public hearings and submitting an annual progress report directly to the US President.
- The NCI director and members of the National Cancer Advisory Board and the President's Cancer Panel be presidential appointees.
- The annual budget of the NCI, called the bypass budget, be submitted directly to the President, bypassing traditional approval by the NIH or the Department of Health and Human Services required of other NIH institutes.

The Act gave the NCI Director broad authority, in consultation with the National Cancer Advisory Board to

- Create new cancer centers and manpower training programs.
- Appoint advisory committees to explore new issues/opportunities.
- Award contracts for research, which were used to create the International Cancer Information Center and other NCI programs.
- Collaborate with other federal, state, or local public agencies and private industry, which is particularly useful for drug screening and establishing numerous partnerships with private industry.
- Conduct cancer control activities, such as antismoking, diet and lifestyle, and early detection programs.
- Establish an international cancer research databank that collects, catalogues, stores, and disseminates results of cancer research undertaken in any country.
- Award research grants.

During the past 25 years, remarkable progress against cancer has been achieved. Improvements in treatment with combination chemotherapy and combined modality therapy through large cooperative randomized trials have led to success in treating several types of cancer. For example, curative therapies were developed for certain types of childhood leukemia, Hodgkin's disease, and testicular cancer. The revolution in the understanding of the molecular basis of cancer is now enabling the development of improved tests for early detection, more precise methods for

diagnosis, more effective strategies for prevention, and more specialized approaches for treatment. Table 2 summarizes some major milestones in the National Cancer Program since 1971.

THE NATIONAL CANCER INSTITUTE TODAY

The Scope of the Cancer Problem

Despite the remarkable progress that has been made in recent decades, cancer remains a significant public health problem. The American Cancer Society estimates that in 1999 more than 1.2 million new cases of cancer will be diagnosed and 563,000 cancer-related deaths will occur. These estimates are based largely on the NCI's Surveillance Epidemiology and End Results Program data.[9] The Surveillance Epidemiology and End Results Program collects and publishes cancer incidence and survival data from population-based cancer registries in various areas of the United States, covering approximately 14% of the population. It also tracks and reports annual cancer mortality data collected by the National Center for Health Statistics. Surveillance Epidemiology and End Results data are the primary data used to monitor the cancer burden and determine emerging trends in the United States.

Between 1990 and 1996, cancer incidence and mortality in the United States for all sites combined declined significantly, reversing an almost 20-year trend of increasing cancer incidence and mortality. The overall 5-year survival rate is approaching 60%. Differential patterns of cancer burden are seen when the data are analyzed according to the factors that have been shown to influence rates, such as race/ethnicity, primary site, sex, age, stage, geography, and social economic status. For example, the cancer incidence rate in black males continues to increase. Nurses interested in reviewing the most current data for preparation of nursing research protocols, presentations, patient education, or planning programs can find the data on the internet (Table 3).

Another effort to assess the nation's cancer burden occurs as part of the US Public Health Service Healthy People Program, which is a collaboration among government, voluntary, and professional organizations, businesses, and individuals. The Healthy People initiative has implemented health promotion and disease prevention objectives to improve the health of the American people.[10] The NCI, the lead agency for monitoring the cancer objectives, organized the Healthy

TABLE 2.

Milestones in the National Cancer Program

1971	The National Cancer Act was signed by President Nixon on December 23
1973	The first eight comprehensive cancer centers were recognized
1973	The Surveillance, Epidemiology, and End Results Program was established to collect and publish statistics on cancer incidence, mortality, and survival for a wide range of racial and ethnic minorities
1974	CANCERLIT, a national computerized service, was developed by the NCI and the National Library of Medicine for scientists to access the latest research findings from the current literature
1975	The Cooperative Minority Biomedical Program was established; now called the Comprehensive Minority Biomedical Program, it provides funding for research training of students in historically black colleges and universities
1976	The Cancer Information Service, a nationwide telephone information and education network, was established; today, the Cancer Information Service receives more than 2,000 calls a day from cancer patients, their families, and the public, and brings NCI messages to undeserved and minority communities through its outreach program
1983	Physician Data Query (PDQ), a computer database that contains current cancer information statements (including disease descriptions and therapies), research studies with new drugs, and directories of physicians and organizations involved in cancer care, went on-line; the database is updated monthly; oncologists, oncology nurses, and other cancer experts are members of the PDQ editorial board
1983	The Community Clinical Oncology Program was launched; community physicians collaborate with scientists conducting NCI-supported studies
1991	The American Stop Smoking Intervention Study for Cancer Prevention program was launched; the world's largest demonstration project for tobacco control is a joint effort between the NCI and the American Cancer Society.
1996	New initiatives; the 1996 bypass budget envisions expansion into four areas of research: cancer genetics, preclinical models of cancer, detection technologies, and developmental diagnostics
1997	The Director's Consumer Liaison Group, the first all-consumer advocate advisory committee at the NCI/NIH, was established
1999	The second cycle of new initiatives is to be funded by the bypass budget

TABLE 3.
Selected National Cancer Institute Websites

Site Address	Information
http://www.nci.nih.gov	Primary web site for the NCI; includes information about the Institute and its programs
http://rex.nci.nih.gov	News, upcoming events, educational materials, and publications for patients, the public, and the mass media
http://www.cancernet.nci.nih.gov	Information for patients and the public, health professionals, and basic researchers; information from PDQ about cancer treatment, screening, prevention, supportive care, and clinical trials; bibliographic information from CANCERLIT
http://cancertrials.nci.nih.gov	Cancer clinical trials information, including how to find specific trials, understanding trials, deciding whether to participate in trials, and research news.
http://www-seer.ims.nci.nih.gov	Surveillance Epidemiology and End Results cancer incidence and survival and mortality data
http://www.nci.nih.gov/cancercenters	Information about the Cancer Centers Program, including links to all centers.
http://deainfo.nci.nih.gov/advisory/boards/htm	NCI advisory boards with charter summary, members, functions and organization, meeting minutes, and annual reports
http://web.health.gov/healthypeople	US Public Health Service Healthy People Program focused on health promotion and disease prevention

People 2000 progress review around three themes: declines in incidence and mortality, disparities in racial and ethnic cancer screening and management, and behavioral indicators. Cancer objectives for Healthy People 2010 are being developed, which will include developing a data collection strategy to further understand factors that put certain racial and ethnic groups at higher risk for cancer, increasing the proportion of investment in behavioral health communications and applied research, developing strategies for increasing participation of racial and ethnic population groups in clinical trials, increasing investment for research to establish the value of intervention, and assuring appropriate attention to children's health issues and environmental risks.

The National Cancer Institute Budget

The NCI is the largest of the 17 biomedical research institutes and centers at the NIH, located in Bethesda, MD. Each year, the NCI prepares the bypass budget to inform the President, Congress, and, through them, the American people about its goals and plans to reduce the cancer burden. The budget is a way to mark progress against cancer, identify the priorities and vision of new opportunities that promise to greatly advance our understanding of this disease, and indicate the resources that will enable the NCI to pursue the most promising avenues of research rapidly and efficiently.[11] The term *bypass budget* is used because the budget request is submitted directly to the President in the fall of each year, bypassing traditional approval by the NIH or the Department of Health and Human Services required of other NIH institutes.[12]

More than two thirds of the budget supports basic and clinical studies conducted across the Nation through the extramural research program. Approximately 16% is spent on the intramural research program; 4% on training, education, and career development of scientists and clinicians; 3% on communicating the latest information about cancer risk, detection, prevention, treatment, rehabilitation, survivorship, and control to people with cancer, health professionals, and the public; and 4% on supporting the administration and management of the institute.

National Cancer Institute Primary Advisory Boards, Groups, and Programs

To ensure the wise use of resources to meet the goals of the National Cancer Program, the NCI actively seeks out expert advice from a variety of advisory bodies from both within and outside of the Institute. Table 4 lists the NCI's primary advisory boards and groups; summarizes their authority, structure, and function; and highlights some recent activities. Complete listings of members of each group reports and meeting minutes are found on the NCI web site (Table 3).

President's Cancer Panel. The President's Cancer Panel was initially established by Congress

TABLE 4.

Selected Advisory Boards and Groups of the National Cancer Institute

Board or Group	Origin	Members	Purpose
President's Cancer Panel	Established by Congress in 1971; reestablished in 1973	Consists of three persons appointed by the President for 3-year terms; two members are distinguished scientists or physicians	Appraise National Cancer Program; monitor development and execution of activities; report directly to the President; bring to the President's attention any delays or blockages in rapid execution of the Program
National Cancer Advisory Board	Originally established as the National Advisory Cancer Council in 1937; renamed and restructured as the National Cancer Advisory Board by the National Cancer Act of 1971; chartered by the Secretary in 1973	NCIs principal advisory body consisting of 18 members appointed by the President and 12 nonvoting ex officio members including the Department of Health and Human Services, Secretary, NCI Director, and leaders of other governmental agencies; since 1991, oncology nursing has been represented	Advises, assists, consults with, and makes recommendations to the Department of Health and Human Services Secretary and NCI Director, performs second level of review for grants and cooperative agreements following technical review
NCI Board of Scientific Advisors	Established by the NCI Director in 1995	Consists of 35 members appointed by the NCI Director, from authorities knowledgeable in the fields of laboratory, clinical and biometric research, clinical cancer treatment, cancer etiology, and cancer prevention and control; oncology nursing is represented on this board	Advises the NCI leadership on the progress and future direction of NCI's Extramural Research Program; evaluates Institute-awarded grants, cooperative agreements, and contracts, and reviews ideas for new research solicitations
Board of Scientific Counselors, NCI	Established by the NCI Director in 1995	Consists of 60 scientists and clinicians from outside NCI and representatives from the consumer advocacy community	Advises the NCI leadership on the progress and future direction of NCI's Intramural Research Program, through periodic site visits and evaluation of intramural laboratories and divisions
NCI Director's Consumer Liaison Group	Established by the NCI Director in 1998; the Director's Consumer Liaison Group (also referred to as "Committee") is governed by the provisions of the Federal Advisory Committee Act	Consists of 15 members appointed by the NCI Director; The members are consumer advocates involved in cancer advocacy and the cancer experience, representing a constituency with which they communicate on a regular basis	Advises and makes recommendations to the NCI Director from the perspective of cancer consumer advocates on a wide variety of issues, programs research priorities, and policy development

on December 23, 1971. It consists of three persons appointed by the President, who by virtue of their training, experience, and background are exceptionally qualified to appraise the National Cancer Program. Members of the Panel, two of whom are distinguished scientists or physicians, are appointed for 3-year terms. The Panel monitors the development and execution of the activities of the National Cancer Program, reports directly to the President, and immediately brings to the attention of the President any delays or blockages in rapid execution of the Program. Public meetings are held at least four times a year, which highlight barriers to making progress in cancer control.

National Cancer Advisory Board. The NCI's principal advisory body, is the Presidentially appointed National Cancer Advisory Board.[13] The National Cancer Advisory Board advises, assists, and consults with the Department of Health and Human Services Secretary and the NCI Director on issues related to the entire National Cancer Program. By law, it provides a second level of review for grant applications referred to NCI and for cooperative agreements under consideration. Deborah Mayer, RN, MSN, AOCN, FAAN, was the first nurse appointed to the board in 1991.

Board of Scientific Advisors and the Board of Scientific Counselors. The Board of Scientific Advisors, along with the Board of Scientific Counselors, represents the scientific community's voice in the science NCI conducts and supports. The Board of Scientific Advisors and the Board of Scientific Counselors are composed of distinguished scientists from outside the NCI and representatives from the consumer advocacy community. The Board of Scientific Advisors advises the NCI leadership on the progress and future direction of the Institute's Extramural Research Program. It evaluates Institute-awarded grants, cooperative agreements, and contracts, and reviews ideas for new research solicitations to ensure that a concept is meritorious and consistent with the Institute's programs. The Board of Scientific Counselors advises the NCI leadership on the progress and future direction of NCI's Intramural Research Program, through reviewing scientific proposals and programs, periodic site visits, and evaluation of intramural laboratories and divisions.

Executive Committee. The NCI Executive Committee includes the chairs of the Board of Scientific Counselors and Board of Scientific Advisors, division directors, and other key advisors to the Director who make major policy and operating decisions for the Institute.

Director's Consumer Liaison Group. In late 1997, the NCI launched a landmark initiative, the Director's Consumer Liaison Group, the NCI's and NIH's first all-consumer advisory committee. It is a chartered advisory committee, giving it the status of a high-level, recognized advisory body that has become a model for increasing consumer involvement at the NIH. The Director's Consumer Liaison Group provides advice and makes recommendations directly to the NCI Director. It helps the NCI increase the representation of the cancer advocacy community on NCI advisory committees and increase their involvement in program and policy development, thereby ensuring that those who experience the burden of cancer also help to shape the course of the NCI's efforts to eradicate this disease. The Director's Consumer Liaison Group, which consists of 15 consumer advocates who are involved in cancer advocacy, some of whom are oncology nurses, is coordinated and supported by the Office of Liaison Activities.

The NCI established the Office of Liaison Activities to strengthen NCI communications and relationships with the cancer advocacy community, scientific and professional organizations, and other federal agencies to better understand their perspectives about the needs of cancer patients, those at risk of cancer, and the public at large. The Office of Liaison Activities, which is the NCI's central point of contact with national advocacy organizations, maintains ongoing communications and information exchange between these organizations and NCI and cooperates and collaborates with these groups in areas of mutual interest. Examples of consumer-driven groups working through the Office of Liaison Activities are the National Breast Cancer Coalition, US TOO (prostate cancer), and the National Coalition for Cancer Survivorship. Professional organizations such as the Oncology Nursing Society and the American Society of Clinical Oncology have increased access to the NCI Director and other NCI leadership through the Office of Liaison Activities.[14]

Cancer Centers Program

The NCI Cancer Centers Program began with the awarding of NCI funds to 12 clinical cancer centers and now includes 58 centers who meet specific standards set by the NCI.[15] There are several distinctions among the centers. Basic science centers conduct laboratory research. Clinical cancer centers conduct both basic and clinical research. A comprehensive status indicates that a center has demonstrated specific strength in basic, clinical, and population studies, interdisciplinary collaboration across scientific boundaries, and provides cancer information, education, and outreach activities for the communities they serve. Consortium centers involve clinical and cancer control research, plus cancer control activities. Traditionally, the NCI cancer centers have been single-institution programs, but more recently the NCI is allowing consortia of institutions linking freestanding clinical and academic centers.

National Cancer Institute Infrastructure for Discovery

The NCI conducts three classes of research: laboratory, clinical, and population. Laboratory research focuses on the biology of cancer, the fundamental properties of cancer-causing agents and mechanisms, and the body's defense against and response to cancer. Clinical research, one of the cornerstones of the National Cancer Program, involves human subjects participating in cancer prevention, detection, diagnosis, treatment, or rehabilitation studies. Population research focuses on the causes, risk factors, predispositions, incidence, and behavioral aspects of cancer. These three settings influence one another. All three classes of research are supported by the NCI infrastructure for discovery. The research is both intramural (conducted at the NCI) and extramural (conducted at centers outside of the NCI). Translational clinical research refers to the application of laboratory findings to the first studies using humans. Translational research is critical to the development of new therapies and is emphasized at NCI clinical and comprehensive centers. The NCI has a major function in the conduct and regulation of clinical cancer research.

History

In 1955, Congress appropriated $5 million to start a contracting function with the NCI for drug development. The Cancer Chemotherapy National Service Center was formed to provide funding through contracts for preclinical testing of compounds for future clinical trials. The program was so successful that by 1965, the contracting function of the Cancer Chemotherapy National Service Center was joined with the intramural chemotherapy research program within the NCI to form the Division of Cancer Treatment.[16] At present the NCI is the largest single sponsor of research on anticancer drugs working with pharmaceutical industry and academic centers.

Community Programs

Two NCI-funded projects were initiated in the 1970s, the Community Oncology Program and the Community Hospital Oncology Program. From these programs, practice guidelines were developed that changed cancer care and led to hospital-based multidisciplinary cancer programs.[17]

Cooperative Groups

The backbone of NCI-sponsored clinical trial research is the cooperative group structure. In the late 1970s, the Cooperative Group Outreach Program (CGOP) was established to enable cooperative groups to familiarize community physicians with clinical research trials. National and regional cooperative clinical trials groups are listed in Table 5. Academic centers are main institutions within the CGOP and regional community institutions are affiliates. The CGOP structure serves to fund academic research programs and is organized to increase collaboration and improve efficiency of clinical research. There are more than 1,700 institutions currently participating in the CGOP and more than 20,000 patients are registered on studies annually. Some cooperative groups are disease focused, such as the National Surgical Adjuvant Breast and Bowel Project; others focus on a treatment modality, such as the Radiation Therapy Oncology Group. The American College of Surgeons Oncology Group is the most recently added group.

The community clinical oncology program was established in 1983. Community clinical oncology programs are community institutions that function more independently than the CGOP affiliates but still receive support from cancer centers. There are 59 community clinical oncology programs in 34 states, with 14 cooperative groups and 17 cancer centers as research bases. The community clinical oncology program structure has been especially helpful in the cancer prevention trials, such as the Prostate Cancer Prevention Trial or the Breast Cancer Prevention Trial.[17,18]

TABLE 5.

National Cancer Institute Cooperative Clinical Trial Groups

Brain Tumor Cooperative Group
Cancer and Leukemia Group B
Children's Oncology Group
Eastern Cooperative Oncology Group
European Organization for Research and Treatment of Cancer
Gynecologic Oncology Group
Intergroup Rhabdomyosarcoma Study
National Surgical Adjuvant Breast and Bowel Project
North Central Cancer Treatment Group
Radiation Therapy Oncology Group
Southwest Oncology Group
The American College of Surgeons Oncology Group

TABLE 6.
Major Advances Resulting From National Cancer Institute Cooperative Group Cancer Research

Cure of childhood acute lymphoblastic leukemia
Cure of Hodgkin's disease
Cure of testicular cancer
Decrease in mortality of childhood cancer
Efficacy of adjuvant treatment of Duke's stage C colorectal cancer
Reduction in mortality of breast cancer

Although CGOPs and community clinical oncology programs differ in structure and research organization, they share the common purpose of developing and conducting large-scale trials in multi-institutional settings. Community physicians can contribute to the national research effort, have access to new drugs, and stay current regarding new treatments by participating in the outreach programs. The cooperative group structure has increased accrual and improved community care of patients with cancer and is credited with a number of advancements in cancer care (Table 6).

Nurses have had an active role in the cooperative groups since their beginning.[19] Cooperative group nurse committees present education programs, establish standards for research nursing and data management, develop symptom management guidelines, and design nursing research protocols. The review of protocols in development by research nurses can identify obstacles to patient accrual and compliance.

Regulatory Review

To deal with the regulatory, scientific, and efficiency issues, the Division of Cancer Treatment developed a Cancer Therapy Evaluation Program, which has the responsibility for reviewing and approving all proposals to conduct clinical trials with compounds for which the NCI is the drug sponsor.[16]

New compounds are tested thoroughly in a preclinical (laboratory) drug development process before an application is made to the Food and Drug Administration for approval of an investigational new drug. This process includes, but is not limited to, procedures to identify the compound, assays to measure chemical and biologic activity, criteria for reproducing the compound, and assessment of preclinical toxicology. Once the drug sponsor has completed the necessary preclinical drug development to obtain investigational new drug approval, a letter of intent is submitted. If the NCI is the sponsor, the Cancer Therapy Evaluation Program will approve the investigational new drug. The investigator then prepares the protocol, which contains essential elements describing the research (Table 7).[16]

At the NCI-designated cancer centers, the regulatory review is a two-step process. The institutional review board reviews the protocol and the consent form to ensure the patient is advised of all risks associated with the research.[20] The Clinical Protocol Monitoring Committee provides a scientific review of the protocol by cancer specialists. Nurses can serve on either committee and play an important role in assessing the feasibility of conducting a protocol. For example, the nurse may determine there will be reimbursement issues, the protocol treatment cannot be administered as described, or patient compliance will be an issue. Once regulatory requirements are met and approval is given, the clinical trial is implemented.

Drug Development

Clinical trials are conducted in phases, each with a different purpose and designed to answer different questions. Phase I trials establish the safety of the new drug or approach in humans. A maximum tolerated dose is established using small groups of patients (cohorts) receiving the same dose. Patients are carefully monitored and all side effects are recorded. Pharmacokinetic data may be collected as well. Other questions, such as the best

TABLE 7.
Elements of a Clinical Trial Research Protocol

Objectives
Background and rationale
Patient eligibility and exclusion criteria
Pharmaceutical information, if applicable
Treatment plan/evaluation plan/intervention or screening plan
Procedures for patient registration and randomization
Dose modification for toxicity, if applicable
Criteria for response assessment, if applicable/outcome evaluation
Patient monitoring schedule
Off-study criteria
Statistical considerations
Records to be kept

way to administer the agent, how often, and for how long, are addressed. Only patients who have no other treatment options are eligible for phase I trials.

Phase II trials establish the anticancer effect of the agent for specific diseases. The patients are carefully monitored for tumor response and alleviation of symptoms. Patients for whom standard therapy does not exist or in whom it no longer works are eligible for phase II trials.

Phase III trials compare the new drug or approach with the standard care to determine whether the new approach is more effective or has less side effects than the standard treatment. If there are several effective treatments for a specific disease, the phase III trials may be compared to determine which is the most effective. Phase III trials include large numbers of patients and are therefore frequently multi-institutional studies.

Obstacles to Cancer Research

In spite of this large and highly organized structure for clinical research, less than 5% of adult patients with cancer enter clinical trials.[21] The cost of research care is a major obstacle to patient participation in clinical trials. Federal funding for cooperative groups is shrinking; it is currently estimated to be 50% of the recommended level.[21] Managed care initiatives have forced the identification of costs specifically related to research and many payers refuse to pay for the "off-label" (not approved by the Food and Drug Administration) use of chemotherapy drugs. Although there are increasing data indicating that the incremental increase in cost of research care is justified, payers frequently refuse to pay for even the standard care associated with a research trial.[16,22,23] Rather than risk payment refusal, the physician may opt to prescribe a standard therapy with less therapeutic efficacy.

Many legislative efforts are ongoing to bring regulation for payment of clinical research costs. The Department of Defense military health system has been a model of collaboration due to a philosophy that access to clinical trials is necessary for a comprehensive approach to cancer care. An intra-agency agreement was signed in 1996 by the Department of Defense and the NCI to allow beneficiaries to participate in phase II or III NCI-sponsored trials.[24] It is the goal of many researchers that all phase III trials sanctioned by the NCI and conducted through the cooperative group organizations be covered by reimbursement.[21] Nurses can advocate legislation to support clinical trials through direct contact with legislators, support of advocacy groups, and participation in professional organizations, such as the Oncology Nursing Society.

Roles of the Research Nurse

The research nurse coordinates all aspects of cancer clinical research.[25,26] The first step is identification of patients for trials through chart screening and patient assessment. The nurse is critical in the informed consent process. The nurse ensures understanding of the treatment plan, risks and benefits of the investigational treatment, what alternative treatments are available, and what the probability is that the patient will receive personal benefit.[27-29] The nurse frequently prepares the consent form for institution review board submission and must ensure that all requirements for the consent form are met (Table 8).

During the implementation of the study, the research nurse is responsible for conducting toxicity assessments at each visit. Toxicity assessments are critical in phase I and II trials since little may be known about expected and unexpected toxicities. All signs and symptoms are assessed, assigned a grading score, and recorded. Identifying and reporting adverse events to the study sponsor is critical to patient safety. The nurse ensures proper procurement and processing of pharmacokinetic samples. Ongoing education of the patient and the patient's caregiver is an essential research nurse role.

Perhaps the earliest NCI activity that impacted nursing directly was initiated in 1948. The nursing sections of the NCI established a formal education program in which the nursing staff of the cancer

TABLE 8.

Elements of Informed Consent

Explanation of the purpose of the research in lay terms
Description of foreseeable risks or discomfort
Description of benefits
Disclosure of appropriate alternative procedures or treatments
Confidentiality of records
Documentation of whether compensation would be available following an injury
Individual to contact about research subject's rights
Statement that participation is voluntary

control branch went to universities to conduct intensive courses for instructors and public health nurses to initiate and strengthen cancer nursing efforts.[30,31]

The NCI has been a leader among the NIH in integrating nurses into its peer-review structures for training and research grants. In addition, there are many funding opportunities for nurses conducting their own research and pursuing additional research training (Table 2).

CHALLENGES FOR THE 21ST CENTURY

The 20th century should be remembered for its progress in translating discoveries and applying them to all populations, in both community and specialized settings, with increased emphasis on prevention, cancer control, and the public's health. In looking toward the future, societal trends will affect application of discoveries. The aging and diversification of the population, for example, has clear public health and cancer control implications. Advances in information technology and mapping the human genome will have significant effects on how cancer care is delivered in the next century. Creativity is needed in applying new knowledge to the benefit of all Americans.

In excess of 40 million people remain uninsured and without meaningful access to care. Even among the insured, application of advances in cancer care and the quality of care delivered vary dramatically. Public health models that distribute benefits to a larger number of people need to be explored in the context of cancer. Great opportunity exists in expanding prevention strategies within public health models. Dr Howard Koh, Massachusetts Commissioner of Public Health, cited tobacco and lung cancer as one of the greatest public health disasters of our time, and expressed hope that we will also remember the 20th century as the end of the "tobacco and cancer" century. In addition, the National Cancer Program of the future must incorporate new communication and education strategies to reduce the cancer burden.

Oncology nurses must continue to contribute to the National Cancer Program in meaningful ways. Adhering to the standards of clinical research, serving on NCI advisory boards and committees, and actively supporting legislative efforts to adequately fund research are all ways for nurses to participate. Continuous self-education about cancer treatment developments, trends, and the barriers to progress will enable nurses to provide leadership in the fight against cancer well into the 21st century.

REFERENCES

1. Knipmeyer MC: Legislative history of the National Cancer Institute. J Natl Cancer Inst 78:1015-1016, 1987
2. Tisevich DA: Legislative history of the National Cancer Institute and the National Cancer Program. Cancer 78:2620-2621, 1996
3. Wynder El, Graham EA: Tobacco smoking as a possible etiologic factor in bronchogenic carcinoma. A study of six hundred and eighty-four proven cases. JAMA 143:329-336, 1950
4. National Cancer Institute: Closing in on Cancer. Publication No. 98-2955. Bethesda, MD, National Institutes of Health, 1998
5. President's Cancer Panel: Genesis and evolution of the National Cancer Program. Statements from the President's Cancer Panel Meeting, July 19, 1999 (http//www.nci.nih.gov)
6. Letton AH: The 25th anniversary of the National Cancer Act. Cancer 78:2597-2598, 1996
7. Davis AC: The legislative process of the National Cancer Act, 1970-71. Cancer 78:2585-2589, 1996
8. Baker CG: Cancer research prior to the National Cancer Act and activities before and after the signing. Cancer 78:2592-2596, 1996
9. Ries LG, Kosary Cl, Hankey BF, et al (eds): SEER Cancer Statistics Review, 1973-1996. Bethesda, MD, National Cancer Institute, 1999
10. Office of Disease Prevention and Health Promotion, US Department of Health and Human Services: Developing Objectives for Healthy People 2010. Washington, DC, Government Printing Office, 1997
11. Director, National Cancer Institute: The Nation's Investment in Cancer Research. Publication No. 98-4373. Bethesda, MD, National Institutes of Health, 1998
12. The National Cancer Act of 1971. J Natl Cancer Inst 78:1031-1038, 1987
13. Lawrence W: The National Cancer Advisory Board—25 years later. Cancer 78:2603-2608, 1996
14. Barr P, Vanchieri C, and the National Cancer Institute Office of Liaison Activities: Understanding Genetic Research and Population-Based Studies. Publication No. 99-4364. National Institutes of Health, 1999
15. Shingleton WW: Cancer centers: Origins and purpose. Arch Surg 124:43-46, 1989
16. Freireich EJ: Societal issues in oncology: Regulatory issues, in DeVita VT, Hellman S, Rosenberg SA (eds): Cancer: Principles and Practice of Oncology (ed 5). Philadelphia, PA, Lippincott-Raven, 1997, pp 2966-2972

17. Einstein AB: Societal issues in oncology: Health care reform, in DeVita VT, Hellman S, Rosenberg SA (eds): Cancer: Principles and Practice of Oncology (ed 5). Philadelphia, PA, Lippincott-Raven, 1997, pp 2957-2966

18. Frelick RW: The community clinical oncology program (CCOP) story: Review of community oncologists' experience with clinical research trials in cancer with an emphasis on the CCOP of the National Cancer Institute between 1982 and 1987. J Clin Oncol 12:1718-1720, 1994

19. Suppers V, Yarbro CH, Mayer-Scogna D: Nursing intervention in clinical research—A model program of nursing contributions to a cooperative study group. Oncol Nurs Forum 6:26-27, 1979

20. Comprehensive Working Group on Informed Consent in Clinical Trials: Recommendations for the Development of Informed Consent Documents for Cancer Clinical Trials. Publication no. 98-4355. Rockville, MD, National Cancer Institute, 1998

21. Comis RL: The cooperative groups: Past and future. Cancer Chemother Pharmacol 42:85-87, 1998 (suppl)

22. Gerszten PC: Oncology in the era of managed care. J Oncol Manage 7:21-23, 1998

23. Brown ML: Cancer patient care in clinical trials sponsored by the National Cancer Institute: What does it cost? J Natl Cancer Inst 91:818-819, 1999

24. Browne D, Baatz LM, Millard F, et al: Oncology Services: The Department of Defense perspective. Cancer 82:2010-2015, 1998 (suppl)

25. Hubbard SM, Donehower MG: The nurse in a cancer research setting. Semin Oncol 7:9-17, 1980

26. Henke C: Emerging roles of the nurse in oncology. Semin Oncol 7:4-8, 1980

27. Cassidy J: The role of the nurse in clinical cancer research. Cancer Nurs 14:124-131, 1991

28. Reese PA, Krebs LU: The nurse's role in the informed consent process. Semin Oncol Nurs 15:116-123, 1999

29. Berry DL, Dodd MJ, Hinds PS, et al: Informed consent: Process and clinical issues. Oncol Nurs Forum 23:507-512, 1996

30. Peterson RI: Federal grants for education in nursing. Nurs Outlook 4:13-15, 1956

31. Jenkins JF, Lake PC: Celebration of an era of public service at the National Institutes of Health and the National Cancer Institute. Cancer Nurs 11:58-64, 1988